AGENDA

On June 28, 2016, information will be presented for expert assessments related to exploring potential pediatric development plans for three products in various stages of development for adult cancer indications. The subcommittee will consider and discuss issues concerning diseases to be studied, patient populations to be included, and possible study designs in the development of these products for pediatric use. The discussion will also provide information to the Agency pertinent to the formulation of written requests for pediatric studies, if appropriate. The products under consideration are: (1) venetoclax, presentation by AbbVie, Inc. (2) tazemetostat, presentation by Epizyme, Inc., and (3) atezolizumab, presentation by Roche/Genentech.

8:00 a.m. Call to Order
Introduction of Subcommittee

Alberto Pappo, MD
Chairperson, Pediatric Subcommittee of the Oncologic Drugs Advisory Committee (ODAC)

8:10 a.m. FDA Introductory Remarks/Presentation

Gregory Reaman, MD
Associate Director for Oncology Sciences
Office of Hematology and Oncology Products (OHOP), Office of New Drugs (OND)
CDER, FDA

8:15 a.m. Topic 1: ABT-199 (Venetoclax) – AbbVie, Inc.

Conflict of Interest Statement
Lauren Tesh, PharmD, BCPS

8:20 a.m. INDUSTRY PRESENTATION

AbbVie, Inc.

Su Young Kim, MD, PhD
Medical Director, Oncology Development
AbbVie, Inc.

8:40 a.m. Clarifying Questions from Subcommittee

8:50 a.m. OPEN PUBLIC HEARING

9:10 a.m. Questions to the Subcommittee and Subcommittee Discussion

10:10 a.m. BREAK

10:25 a.m. Topic 2: Tazemetostat – Epizyme, Inc.

Conflict of Interest Statement
Lauren Tesh, PharmD, BCPS
### AGENDA (cont.)

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<tr>
<th>Time</th>
<th>Session</th>
<th>Presenter(s)</th>
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<tr>
<td>10:30 a.m.</td>
<td><strong>INDUSTRY PRESENTATION</strong></td>
<td>Epizyme, Inc.</td>
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<td>Tazemetostat for the Treatment of Pediatric Subjects with Malignant</td>
<td>Peter Ho, MD, PhD</td>
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<td>Rhabdoid Tumors and Other INI1-Negative Tumors</td>
<td>Chief Medical Officer</td>
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<td>Epizyme, Inc.</td>
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<td>10:50 a.m.</td>
<td>Clarifying Questions from Subcommittee</td>
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<td>11:00 a.m.</td>
<td><strong>OPEN PUBLIC HEARING</strong></td>
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<td>11:20 p.m.</td>
<td>Questions to the Subcommittee and Subcommittee Discussion</td>
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<td>12:20 p.m.</td>
<td><strong>LUNCH</strong></td>
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<td>1:20 p.m.</td>
<td><strong>Topic 3: Atezolizumab- Roche/Genentech</strong></td>
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<td>Conflict of Interest Statement</td>
<td>Lauren Tesh, PharmD, BCPS</td>
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<td>1:25 p.m.</td>
<td><strong>INDUSTRY PRESENTATION</strong></td>
<td>Roche/Genentech</td>
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<td>Atezolizumab Oncology Development</td>
<td>Raphaël Rousseau, MD, PhD</td>
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<td>Global Head, Pediatric Oncology Drug Development Group</td>
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<td>Genentech, a member of the Roche Group</td>
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<td>1:45 p.m.</td>
<td>Clarifying Questions from Subcommittee</td>
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<td>1:55 p.m.</td>
<td><strong>OPEN PUBLIC HEARING</strong></td>
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<td>2:15 p.m.</td>
<td>Questions to the Subcommittee and Subcommittee Discussion</td>
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<td>3:15 p.m.</td>
<td><strong>ADJOURNMENT</strong></td>
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On June 29, 2016, during the morning session, information will be presented for expert assessments related to exploring potential pediatric development plans for two products in various stages of development for adult cancer indications. The subcommittee will consider and discuss issues concerning diseases to be studied, patient populations to be included, and possible study designs in the development of these products for pediatric use. The discussion will also provide information to the Agency pertinent to the formulation of written requests for pediatric studies, if appropriate. The products under consideration are: (1) LOXO-101, presentation by Loxo Oncology, Inc., and (2) entrectinib, presentation by Ignyta, Inc.

During the afternoon session, information will be presented on the current unmet clinical need in the nearly uniformly fatal brain tumor, diffuse intrinsic pontine glioma (DIPG) which occurs predominantly in the pediatric age group. The diagnosis of DIPG is typically based on characteristic radiographic and clinical features in lieu of brain biopsy, and histological confirmation. Recent data has demonstrated that the biology and pathophysiology of these tumors differ. There are no approved drugs for this disease. Clinical investigators seek to exploit precision medicine approaches to DIPG and use potentially predictive information from the genomic signature of tumors at either diagnosis or relapse. This information can be used to select specific molecularly targeted drugs based on the genetic aberrations of an individual patient’s tumor. The Agency will seek the input of the subcommittee, including an assessment of benefit/risk given the potential for an adverse event associated with a surgical intervention in the brainstem.

8:00 a.m.  Call to Order
Introduction of Subcommittee

Alberto Pappo, MD
Chairperson, Pediatric Subcommittee of the Oncologic Drugs Advisory Committee (ODAC)

8:10 a.m.  FDA Introductory Remarks/Presentation

Gregory Reaman, MD
Associate Director for Oncology Sciences, Office of Hematology and Oncology Products (OHOP), Office of New Drugs (OND)
CDER, FDA

8:15 a.m.  Topic 1: LOXO-101- Loxo Oncology, Inc.

Conflict of Interest Statement

Lauren Tesh, PharmD, BCPS
Designated Federal Officer, ODAC

8:20 a.m.  INDUSTRY PRESENTATION

Loxo Oncology, Inc.

Developing LOXO-101 in Children with NTRK Gene Fusion Cancers

Josh Bilenker, MD
Chief Executive Officer
Loxo Oncology, Inc.

8:40 a.m.  Clarifying Questions from Subcommittee

8:50 a.m.  OPEN PUBLIC HEARING

9:10 a.m.  Questions to the Subcommittee and Subcommittee Discussion
10:10 a.m.  **BREAK**

10:20 a.m.  **Topic 2: Entrectinib – Ignyta, Inc.**  
Conflict of Interest Statement  
Lauren Tesh, PharmD, BCPS

10:25 a.m.  **INDUSTRY PRESENTATION**  
Entrectinib for the Treatment of Pediatric Cancers Harboring an Activating Alteration of NTRK1/2/3, ROS1, or ALK  
Pratik S. Multani, MD, MS  
Chief Medical Officer at Ignyta, Inc.

10:45 a.m.  Clarifying Questions from Subcommittee

10:55 a.m.  **OPEN PUBLIC HEARING**

11:15 p.m.  Questions to the Subcommittee and Subcommittee Discussion

12:15 p.m.  **LUNCH**

1:15 p.m.  **Topic 3: Diffuse Intrinsic Pontine Glioma (DIPG)**  
Conflict of Interest Statement  
Lauren Tesh, PharmD, BCPS

1:20 p.m  FDA Introductory Remarks  
Joohee Sul, PhD  
Medical Officer  
Division of Oncology Products II (DOPII)  
OHOP, OND, CDER, FDA

1:25 p.m.  **FDA PRESENTATIONS**  
To Biopsy or Not to Biopsy – That is the Question.  
Robert (Skip) Nelson, MD  
Deputy Director and Senior Pediatric Ethicist  
Office of Pediatric Therapeutics  
Office of the Commissioner, FDA

Biopsy Risks for Investigational in vitro Diagnostic Devices  
Jeffrey D. Seidman, MD  
Medical Officer/Pathologist  
Molecular Pathology and Cytology Branch  
Division of Molecular Genetics and Pathology  
Office of In Vitro Diagnostics and Radiological Health  
Center for Devices and Radiological Health  
FDA
2:10 p.m. **SPEAKER PRESENTATION**

Treatment Opportunities in Diffuse Intrinsic Pontine Glioma (DIPG)  
**Mark W. Kieran, MD, PhD**  
Director, Pediatric Medical Neuro-Oncology  
Dana-Farber Cancer Institute/Boston Children’s Hospital  
Director, Pediatric Brain Tumor Clinic  
Dana-Farber Cancer Institute/Boston Children’s Hospital  
Associate Professor of Pediatrics  
Harvard Medical School

2:25 p.m. **GUEST SPEAKER PRESENTATIONS**

DIPG: The Role of Neurosurgery  
**Jeffrey R. Leonard, MD**  
Pediatric Neurosurgeon  
Chief of Neurosurgery  
Nationwide Children’s Hospital  
Professor, Department of Neurological Surgery  
The Ohio State University

Surgical Experience with Biopsy of Brainstem Tumors  
**Nalin Gupta, MD, PhD**  
Professor in Residence of Neurological Surgery and Pediatrics  
Dennis Bruce Dettmer Endowed Chair in Pediatric Neurosurgery  
Director, Pediatric Neurological Surgery Program  
Principal Investigator, Brain Tumor Research Center  
University of California, San Francisco

Clarifying Questions from Subcommittee

2:50 p.m. **BREAK**

3:05 p.m. **OPEN PUBLIC HEARING**

3:25 p.m. Questions to the Subcommittee and Subcommittee Discussion

4:25p.m. Closing Remarks  
**Gregory Reaman, MD**

4:30 p.m. **ADJOURNMENT**